Citation:

Pepino MY, Mennella JA. Effects of breast pumping on the pharmacokinetics and pharmacodynamics of ethanol during lactation. *Clin Pharmacol Ther.* 2008; 84(6): 710-714.

PubMed ID: 18596681

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To determine whether breast pumping one hour before drinking contributes to lactation-related changes in ethanol pharmacokinetics and pharmacodynamics
- To determine whether these effects of pumping are more pronounced when ethanol is consumed after a meal.

Inclusion Criteria:

16 lactating women at three to five months postpartum.

Exclusion Criteria:

- Pregnancy, alcohol dependence or abstinence, diabetes, obesity and tobacco use
- At 8:30 A.M. on each day, pregnancy tests were administered, breath carbon monoxide was measured to verify non-smoking status and capillary blood glucose levels were measured to ensure that subjects had abstained from eating since the previous night.

Description of Study Protocol:

Recruitment

Unclear.

Design

- A within- and between-subject design study. The within-subject factor was the testing condition (fed or fasted), and the between-subject factor was the experimental group (PB or PA)
- Both groups used an electric breast pump (Medela, Crystal Lake, IL) for 16 minutes (eight

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minutes per breast) on two test days separated by one week. Subjects randomly assigned to group PB (N=8) breast pumped an hour before drinking, whereas those assigned to group PA (N=8) breast pumped 0.6 hours after drinking, having last nursed or breast pumped 2.6±0.7 hours prior to ethanol consumption.

- At approximately 9:00 A.M. (shortly after group PB finished pumping) and in counterbalanced order, the subjects ingested a standard meal (530kcal) on one test day (fed condition) and continued to fast during the other (fasted condition). This standard meal was ingested within 10 minutes. One hour later (time zero), the subjects drank a 0.4g per kg dose of ethanol in a palatable, non-caloric, strawberry-kiwi-flavored drink. The alcoholic beverage (15% vol per vol) was aliquoted into two equal volumes, each consumed within consecutive five-minute periods. Blood ethanol concentrations (BECs) estimated from breath (Alco-Sensor IV, St. Louis, MO) and ear temperatures (Braun, Kronberg, Germany) were measured before and at fixed intervals after (beginning at 0.4 and ending at 3.4 hours) drinking. Subjects also completed the Biphasic Alcohol Effects Scale before (-0.5 hours) and after (0.4, 0.9, 1.4 and 2.9 hours) drinking to determine whether breast pumping altered feelings of stimulation and sedation across the BEC curve.

Intervention

- 16 lactating women three to five months postpartum participated in the study
- A within- and between-subjects design was conducted. The within-subjects factor was testing condition (fed or fasted) and the between-subjects factor was experimental group (PB or PA).
- Both groups used an electric breast pump for 16 minutes (eight minutes per side) on two test days separated by one week. Subjects were randomly assigned to the PB (pumped an hour before drinking) or PA (pumped 0.6 hours after drinking) group. The same intensity setting on the pump was used for each women.
- Subjects ingested (counterbalanced order) a standard meal (530kcal) on one test day and continued to fast on the other test day. One hour later women drank 0.4g per kg dose of ethanol in a palatable, non-caloric strawberry-kiwi flavored drink.
- BEC was estimated by breath and ear temperatures were measured before and at fixed intervals after (beginning at 0.4 and ending at 3.4 hours) drinking. Subjects completed the Bi-phasic Alcohol Effects Scale before (0.5 hours) and after (0.4, 0.9, 1.4 and 2.9 hours) after drinking to determine whether breast pumping altered feelings of stimulation and sedation across the BEC curve.

Statistical Analysis

- Dependent variables included BEC levels, classic pharmacokinetic parameters, ear temperatures, and feelings of stimulation and sedation. Separate mixed analyses of variance were carried out for each dependent variable, with group (PB or PA) as the between-subject factor, and condition (fed or fasting) and time since ethanol consumption (where applicable) as within-subject factors. Peak BEC was a covariate for Biphasic Alcohol Effects Scale analyses to ensure that any group differences were not due to BEC differences.
- When analyses of variance revealed significant effects, post hoc Fisher least significant difference analyses were conducted. If the sphericity assumption of the analysis of variance was violated, Geisser corrections were used. All analyses were performed using STATISTICA (StatSoft, Tulsa, OK), and the criterion for statistical significance was $P \leq 0.05$.

Data Collection Summary:

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Dependent Variables

- Variable one: Peak blood ethanol concentration (BEC), time-to-peak BEC, and area under the blood ethanol–time curve (AUC; g per hour per L). AUCs were estimated using a software program (OriginLab, Northampton, MA) based on the trapezoidal rule. Two AUCs were calculated for each condition. One focused on the entire session ($AUC_{0–3.4\ h}$), and the other on the time from ethanol ingestion (time zero) until 0.6 h ($AUC_{0–0.6\ h}$), the time after which group PA began pumping. Thus, any group differences in $AUC_{0–0.6\ h}$ would be due to the fact that one group breast pumped before ethanol ingestion whereas the other did not.
- Ear temperatures
- Feelings of stimulation and sedation (Biphasic Alcohol Effects Scale).

Independent Variables

- Fed vs. fasted
- Pumped before or pumped after ethanol consumption.

Description of Actual Data Sample:

- *Initial N:* 16
- *Attrition (final N):* 16
- *Age:* 33.3±1.0 and 32.3±1.7 years
- *Other relevant demographics:* There were no significant (NS) differences between the two groups in:
  - Pregnancy length (38.3±1.5 and 39.2±0.7 weeks)
  - Time since parturition (4.0±0.3 and 4.5±0.3 months)
  - Age
  - Drinking habits (5.5±2.7 and 4.1±1.0 standard drinks during the past three weeks)
  - How women fed their babies
- *Anthropometrics:* Body mass index (BMI) (22.0±0.7 and 24.6±1.1kg/m^2) was NS different
- *Location:* Philadelphia, Pennsylvania, US.

Summary of Results:

Findings

- Blood ethanol concentrations (BECs) significantly changed over time ($P<0.001$) and the pattern of change was significantly dependent on the timing of breast pumping (main effect of group, $P<0.05$; hypothesis one), and on whether the ethanol was consumed before or after a meal (main effect of condition: $P<0.001$)
- During the fed condition, BEC levels were significantly lower ($P<0.001$) and tended to peak later ($P=0.06$)
- Considering the first hypothesis, women who pumped before drinking (group PB) had lower peak BECs ($P=0.01$) and reduced systemic availability of ethanol, as evidenced by the smaller AUC0−0.6 hours ($P=0.05$). Those who did not breast pump until 0.6 hours after drinking (group PA) eliminated ethanol faster, as determined by β60 ($P=0.008$), b60 ($P=0.008$) and R ($P=0.05$).
- Eating a meal before drinking ethanol significantly reduced the systemic availability of ethanol by 38%. If the women also breast pumped within the hour before drinking,

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availability was reduced even further (58%).

Other Findings

- The timing of breast pumping relative to ethanol consumption also affected body temperatures (P=0.05). Ethanol consumption decreased temperatures 1.3 to 1.9 hours later in group PB. Overall temperatures were lower during fasted than fed conditions in group PB only (P<0.01).
- Both groups felt ethanol's sedative effects during the fed (P=0.005) and the fasted (P<0.001) conditions and felt its stimulant effects during the fasted condition (P=0.02). However, the groups differed in how stimulated they felt when ethanol was consumed after a meal (P=0.03).
- Only group PA felt the stimulant effects of ethanol during the immediate hour after drinking as compared to baseline. The stimulatory effects persisted even after controlling for group differences in BEC (P<0.01). Feelings of sedation were not significantly correlated with feelings of stimulation, which is consistent with the contention that the biphasic effects of ethanol function independently.

Author Conclusion:

Eating a meal before drinking reduced ethanol's systemic availability, and if lactating women also breast pumped before drinking, systemic availability of ethanol was reduced further. This suggests that food and breast stimulation have additive effects on ethanol metabolism.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes

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1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No

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4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

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7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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